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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,785	12/29/2000	John Nelson	41934/23838	4216

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,785	NELSON ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-10 and 12-27 are pending.

Applicants' amendment filed January 9, 2004 is acknowledged, and applicants' response has been fully considered. Claim 5, 6, 24 and 25 have been amended. Therefore, claims 1-10 and 12-27 are examined. A proposed Examiner's Amendment has been faxed to the applicant on April 13, 2004, but it has not been accepted by the applicant.

Objection Withdrawn

2. The previous objection to the disclosure is withdrawn in view of applicants' amendment to the specification, and applicants' response at pages 11-12 in the amendment filed January 9, 2004.

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 5-8, 12-18 and 24-27, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at pages 17-19 in the amendment filed January 9, 2004.

4. The previous rejection of claims 5-8, 12-18 and 24-27, under 35 U.S.C.112, first paragraph, is withdrawn in view of applicants' amendment to the claim, applicants' response at pages 12-17, and the references provided in the amendment filed January 9, 2004.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-4, 9, 10 and 19-23 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a peptide factor. As written, the claim does not explicitly indicate the hand of man. Insertion of "isolated" or "synthetic" in connection with a peptide factor is suggested. See MPEP § 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-10 and 12-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of murine epidermal growth factor (m-EGF, SEQ ID NO:2) having tyrosine substituted with a tyrosine analog, or arginine substituted with an arginine analog, and optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, or, replacement of a peptide bond with a protease-resistant peptide bond isostere, replacement of a glycine residue with α,α-dialkyl substituted amino acid, or stabilization of a helical turn of the peptide using intra chain linkers; or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor, does not reasonably provide enablement for a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine substituted with a tyrosine analog, or at least one arginine substituted with an arginine analog, optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, replacement of a peptide bond with a protease-resistant peptide bond isostere, replacement of a glycine residue with α,α-dialkyl substituted

amino acid, or stabilization of a helical turn of the peptide using intra chain linkers, where more modifications other than substitution at Tyr or Arg of residues 33 to 42 of mEGF are not identified; or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-10 and 12-27 encompass a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine substituted with a tyrosine analog, or at least one arginine substituted with an arginine analog, optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, replacement of a peptide bond with a protease-resistant peptide bond isostere, replacement of a glycine residue with α,α-dialkyl substituted amino acid, or stabilization of a helical turn of the peptide using intra chain linkers (claims 1-4, 9, 10 and 19-23); or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor (claims 5-8, 12-18 and 24-27). The specification, however, only discloses cursory conclusions without data supporting the findings, which state that a peptide factor derived from amino acid residues 33-42 of mEGF with at least one substitution of tyrosine at position 5 or of arginine at position 9 can be used as a medicament for treatment of angiogenic disease via its binding to 67 kDa laminin receptor (pages 2-3). There are no indicia that the present application enables the full scope in view of a modified peptide factor derived from amino acid residues 33-42 of mEGF, and a method of agonizing or antagonizing a laminin receptor using the modified peptide factor as discussed in the stated rejection. The factors considered in determining whether undue

experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the peptide factor comprising the modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine substituted with a tyrosine analog, or at least one arginine substituted with an arginine analog, where more modifications other than substitution at Tyr or Arg of residues 33 to 42 of mEGF are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification indicates the peptide substitution in Tables 1a and 1b, and there are no working examples indicating the peptides containing one tyrosine or arginine substitution have more modifications other than capping N-terminal, C-terminal or cysteine residue.

(3). The state of the prior art and relative skill of those in the art:

The prior art (Nelson et al., J. Biol. Chem. 271, 26179-26186 (1996)) indicates a laminin-antagonist peptide comprising amino acid residues 33-42 of mEGF interacts with a 67 kDa laminin receptor of breast cancer and endothelial cell. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific teachings on identities of modified peptides containing more modifications than Tyr or Arg substitution and capping N-terminal, C-terminal or cysteine residue, and the effects of

these peptide factors in agonizing or antagonizing a laminin receptor to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine or arginine substitution, and optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor, however, the identities of the peptides containing more modifications than Tyr or Arg substitution, and the effects of these peptide factors as agonists or antagonists to a laminin receptor are not adequately described in the specification, the invention is highly unpredictable regarding the effects of various modified peptide factors in agonizing or antagonizing a laminin receptor.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine or arginine substitution, and optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor. The specification indicates a series of peptides (Tables 1a and 1b) derived from mEGF(33-42) have been synthesized and used for testing receptor interaction with laminin receptor, cell adhesion and motility properties in vitro (pages 8-20, Example 2), and amino acid residues at certain positions are found to be essential for antagonist activity, e.g., the

H-bonding between tyrosine (P5) and the arginine (P9) (paragraph 0094). However, the specification has not identified various peptide factors containing more modifications than a Tyr or Arg substitution, nor has demonstrated the effects of these peptide factors in agonizing or antagonizing laminin receptors. Moreover, there are no working examples demonstrating the effects of these peptide factors. Since the specification fails to provide sufficient teachings on the identities of the peptides containing more modifications than Tyr or Arg substitution, and the effects of these peptide factors as agonists or antagonists to a laminin receptor, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of these peptide factors in agonizing or antagonizing laminin receptors.

(6). Nature of the Invention

The scope of the claims encompasses a peptide factor comprising a modified peptide of amino acid residues 33 to 42 of mEGF having at least one tyrosine or arginine substitution, or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor, however the specification has not provided sufficient teachings on various peptide factors containing more modifications other than a tyrosine or arginine substitution and capping N-terminal, C-terminal or cysteine residue. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working examples do not demonstrate the claimed variants and methods associated with variants, the teachings in the specification are limited, and the effects of peptide factors are unpredictable, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of the modified peptide factors in agonizing or antagonizing a laminin receptor.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-10 and 12-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1-10 and 12-23 are indefinite because the claim recites amino acid residues 33 to 42 of murine epidermal growth factor without providing a reference "SEQ ID NO:", it is not what amino acid sequence the residues are referred to. Claims 1-10 and 12-23 are also indefinite because the claim recites the peptide factor comprising amino acid residues 33-42 of murine epidermal growth factor, which is the natural peptide, however, it also indicates the peptide factor is modified in step a), it is not clear which peptide factor binds to laminin receptors in step b), the natural or the modified one. Claims 2-4, 7-10, 13-18, 22 and 23 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

9. Claims 19-27 are indefinite because of the use of the term "substitution of at least one murine epidermal growth factor tyrosine.....and substitution of at least one murine epidermal growth factor arginine.....arginine analogue". Note that Markush group (selected the group consisting of) must be closed and "substitution of at least one.... " is open language in regard to the number of substitution. Claims 22, 23, 26 and 27 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

Conclusions

10. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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April 17, 2004